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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/776,768	02/06/2001	Stephen P.A. Fodor	56297-5009	3913

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EXAMINER
SIEW, JEFFREY

ART UNIT	PAPER NUMBER
1637	22

DATE MAILED: 07/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/776,768	FODOR ET AL.	
	Examiner	Art Unit	
	Jeffrey Siew	1637	

-- The MAILING DATE of this communication appears n the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 June 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-44* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *29 June 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Priority

1. If applicant desires priority under 35 U.S.C. 120 based upon a previously filed application, specific reference to the earlier filed application must be made in the instant application. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph unless it appears in an application data sheet. **The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. _____" should follow the filing date of the parent application.** If a parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time

period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

The response states that the preliminary amendment cites the parent lineage. However, the status of each parent application should be updated.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or

> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

Claims 25-27,30-37, 39 & 42 are rejected under 35 U.S.C. 102(e) as being anticipated by Southern et al (6,054,270 April. 25, 2000).

Southern teach a method of detecting a mutation in target nucleic acid versus a known sequence comprising screening target sequence by exposing target sequence to at least one known core sequence probe, determining absolute binding affinity of target sequence to known core sequence probe thereby detecting mutation (see whole doc. esp. abstract & example 3 "array with multiple oligonucleotides including 19mer oligonucleotide compare hybridization affinity against a temperature gradient thereby detecting mismatches"). They detect thru scanning autoradiographic images (see col. 8 line 45-53). They also teach 11, 12 and 13 oligomers (see col.9 line 42). They teach detection of sickle cell anemia mutation (see Example 4 & col.11 lines 6-15 where target β-globin gene is screened), The teach detection of cystic fibrosis (see col.3 line 8).

The terms "core sequence probe" and absolute binding affinity" read broadly on Southern's array probes and his measurement of resulting hybridization of targets .

The response filed 6/5/03 has been fully considered and deemed not persuasive. The response states that Southern et al do not teach any "known" core sequence probes", "determining binding affinity" or "comparing binding affinity of known core sequence probe to target and a known sequence". They further states that no where could be located " array of multiple oligonucleotides including 19mer oligonucleotide compare hybridization affinity against temperature gradient thereby detecting mismatches" in the Southern reference. First, the terms "known core sequence probes" and "binding affinity" are applicants chosen words. A

review of the instant application does not reveal any particular limitation or definition to such terms. As such the terms are interpreted in their logical and commonly known meanings to one skilled in the art. Southern et al oligonucleotide probes particularly the wild type probes would satisfy the limitation of known core sequence as the sequences of the wild type probes were known and constructed to hybridize to the wild type target. Second, Southern's measure of the complementariness of two strands in the process of hybridization during the melting is a measure of binding affinity. The instant specification does not particularly limit the term to a specific type or methodology of measurement. Moreover Southern do teach a comparison of probes with targets over a temperature range (see col. 10 lines 55-65).

The response further argues that Southern do not teach the same determination of binding affinity as required in the instant claims because Southern et al relies on detecting only perfectly matched sequence targets and that there is no comparison of binding affinities. However, Southern does a comparison between the differently matched targets and compares their melting behavior (see col. 11 line 25-30). The claims read broadly and would encompass Southern et al's measure of hybridization using melting temperatures to distinguish mismatches. The melting behavior measures the level of complementariness between the strands which in turn is a measure of their binding affinity. The art rejections over principal Southern rejections are therefore maintained. It may prove helpful to insert limitations into the steps of measuring the binding affinity to further distinguish the type of measurement over Southern. However, such limitations may require new search and consideration.

Claim Rejections - 35 USC § 103

3. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claim 38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Southern (6,054,270 April. 25, 2000) in view of Shuber (US5,633,137 May 27 1997).

The teachings of Southern are described previously.

Southern do not teach P-53.

Shuber teach ASO probes for detection of mutations in P-53 (see whole doc. esp. col.1 line37 & col.4 line 19).

One of ordinary skill in the art would have been motivated to apply Shuber's probes to Southern et al's array in order to detect mutations in P-53 genes. As Shuber explicitly teach the different sequences of probes to detect disease mutations in P-53, a reasonable expectation of

success would exist in applying these probes to Southern's oligonucleotide array. It would have been prima facie obvious to combine Southern's array and Shuber et al's probe in order to screen and detect the mutations in disease gene sequence in target samples.

4. Claims 40 & 41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Southern et al (6,054,270 April. 25, 2000) in view of Owerbach (US4,965,189 Oct 23, 1990).

The teachings of Southern are described previously.

Southern do not teach DQ-beta gene.

Shuber teach probes for detection of mutations in DQ beta gene (see whole doc. esp. abstract).

One of ordinary skill in the art would have been motivated to apply Owerbach probes to Southern et al's array in order to detect mutations in DQ-Beta genes. As Owerbach explicitly teach the different sequences of probes to detect disease mutations in DQ-beta gene, a reasonable expectation of success would exist in applying these probes to Southern's oligonucleotide array. It would have been prima facie obvious to combine Southern's array and Owerbach's probe in order to screen and detect the mutations in DQ-beta gene sequence that show a predisposition to diabetes mellitus in individuals.

5. Claims 43 is rejected under 35 U.S.C. 103(a) as being unpatentable over Southern et al (6,054,270 April. 25, 2000) in view of Erlich et al (US5,468,613 Nov. 21, 1995).

The teachings of Southern are described previously.

Southern do not teach DQ-beta gene.

Southern do not teach forensics.

Erlich et al teach probe hybridization in forensic analysis.(see whole doc. esp. col4 line 53).

One of ordinary skill in the art would have been motivated to apply Erlich et al' teaching of forensic applications to Southern's hybridization assay in order to perform forensic analysis on individuals. As Erlich teach that polymorphic determinations are useful for forensic analysis, it would have been prima facie obvious to combine Erlich et al's motivation to determine sequences in forensic analysis to Southern's array which identify individuals.

6. Claims 28 & 29 are rejected under 35 U.S.C. 103(a) as being unpatentable over Southern et al (6,054,270 April. 25, 2000) in view of Fodor et al (US5,324,633 June 28, 1994).

The teachings of Southern are described previously.

Southern do not teach plotting and normalization.

Fodor et al teach plotting the binding affinity results of fluorescence assays on graph and normalized. (see col.7 line 9-26 & Figure 6).

One of ordinary skill in the art would have been motivated to apply Fodor et al's teachings of fluorescence plots to Southern's array results in order to plot the binding affinity of the probes with targets. As it was well known and commonly practiced in the art to plot the data results, it would have been prima facie obvious to apply Fodor et al's teaching of normalized plots to Southern probe arrays in order to examine the binding results of the different probes and correlate with the target sequence.

SUMMARY

7. No claims allowed.

Conclusion

8. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

CONCLUSION

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Siew whose telephone number is (703) 305-3886 and whose e-mail address is Jeffrey.Siew@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route. The examiner is on flex-time schedule and can best be reached on weekdays from 6:30 a.m. to 3 p.m. If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703)-308-1119.

Any inquiry of a general nature, matching or filed papers or relating to the status of this application or proceeding should be directed to the Tracey Johnson for Art Unit 1637 whose telephone number is (703)-305-2982.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Center numbers for Group 1600 are Voice (703) 308-3290 and FAX (703)-308-4242.

JEFFREY SIEW
PRIMARY EXAMINER

July 25, 2003